Variable Effects of Soy Protein on Plasma Lipids in Hyperlipidemic and Normolipidemic Hemodialysis Patients

Shu-Tzu Chen, MS, Shyang-Hwa Ferng, MD, Chwei-Shiun Yang, MD, Sheng-Jeng Peng, MD, Huei-Rong Lee, MS, and Jiun-Rong Chen, PhD

• ***Background:*** **Hyperlipidemic factors contribute to the high cardiovascular risk in hemodialysis patients. Soy protein has decreased some atherogenic lipid concentrations in subjects with normal renal function. This study evaluates the effect of soy protein on serum lipid profiles in hyperlipidemic and normolipidemic hemodialysis patients.** ***Methods:*** **Nineteen hyperlipidemic and 18 normolipidemic hemodialysis patients were enrolled in a randomized, double-blind, placebo-controlled, clinical trial. After a 4-week run-in phase, subjects in each category were randomly assigned to 2 groups. Thirty grams of isolated soy protein or milk protein was consumed daily as a beverage at breakfast or postdialysis for 12 weeks.** ***Results:*** **In hyperlipidemic subjects, soy protein intake significantly decreased total cholesterol levels by 18.6% (95% confidence interval [CI], −11.4 to −25.8; $P = 0.04$), triglyceride levels by 43.1% (95% CI, −34.0 to −52.2; $P = 0.02$), non–high-density lipoprotein cholesterol levels by 23.6% (95% CI, −14.7 to −32.5; $P < 0.01$), apolipoprotein B levels by 15.4% (95% CI, −5.4 to −25.4; $P = 0.01$), and insulin levels by 49.8% (95% CI, −23.3 to −66.1; $P < 0.01$). Low-density lipoprotein cholesterol concentration was decreased significantly (−25.8%; 95% CI, −8.3 to −42.7; $P = 0.01$), and high-density lipoprotein cholesterol level was increased significantly (17%; 95% CI, 2 to 32.0; $P = 0.03$), but there was no significant difference compared with the milk protein group (−5.5% ± 16.9% and 7.0% ± 11.8%, respectively). There were no significant changes in serum lipid and lipoprotein concentrations in normolipidemic subjects.** ***Conclusion:*** **These results indicate soy protein substitution has lipid-lowering effects in hyperlipidemic hemodialysis patients. However, soy protein intake had little effect on plasma lipid levels in normolipidemic hemodialysis patients.** ***Am J Kidney Dis*** **46:1099-1106.**

INDEX WORDS: Soy protein; hemodialysis (HD); lipoprotein; apolipoprotein; triglyceride; cholesterol; lipid.

PATIENTS ON MAINTENANCE hemodialysis treatment are at elevated atherogenic risk, and hyperlipidemia appears to be one of the major risk factors.[1] Management of hyperlipidemia is one of the important therapeutic goals for hemodialysis patients.[2,3] The National Cholesterol Educational Program Step I diet, which restricts fat intake (<30% of total calories), usually is recommended as an initial treatment to decrease serum lipid levels.[4] However, patients on hemodialysis therapy have a number of other nutritional concerns,[5] and it is difficult to decrease fat intake to less than 30% of total calories in the usual hemodialysis diet. The diet usually prescribed for maintenance hemodialysis patients contains high-protein (>1.2 g/kg/d).[5] Foods containing proteins are major sources of dietary fats and cholesterol.[6] Research showed that soy protein intake improved lipid profiles and enhanced the hypocholesterolemic effect of the National Cholesterol Educational Program Step I diet in hypercholesterolemic individuals with normal renal function[6-10] and patients with nephrotic syndrome and diabetic nephropathy.[11-13] However, the effect of soy protein in normolipidemic subjects is conflicting.[10,14-16] There are reports in the literature that hypocholesterolemia is associated with greater mortality in maintenance hemodialysis patients.[17,18] Because of the limited data available, it is unclear whether soy protein has a clinically relevant and beneficial effect on plasma lipid level management in hemodialysis patients.

In this clinical trial, we examine the effects of soy protein consumption on lipid metabolism in hemodialysis patients and evaluate the lipemic re-

From the Department of Nutrition and Health Sciences, Taipei Medical University; and Divisions of Nephrology and Nutrition, Cathay General Hospital, Taipei, Taiwan.

Received June 27, 2005; accepted in revised form August 25, 2005.

Originally published online as doi:10.1053/j.ajkd.2005.08.031 on October 21, 2005.

Supported in part by a Cathay General Hospital Research Grant.

Address reprint requests to Jiun-Rong Chen, PhD, Department of Nutrition and Health Sciences, Taipei Medical University, No. 250 Wu-Hsin St, Taipei 110, Taiwan. E-mail: syunei@tmu.edu.tw

0272-6386/05/4606-0012$30.00/0

doi:10.1053/j.ajkd.2005.08.031

sponse between normolipidemic and hyperlipidemic subjects.

METHODS

Patients

Nondiabetic maintenance hemodialysis patients from the Hemodialysis Center of Cathay General Hospital, Taipei, Taiwan, were recruited for this randomized, double-blind, placebo-controlled, clinical trial. Criteria for enrollment as normolipidemic subjects included a fasting plasma total cholesterol (TC) concentration between 150 and 200 mg/dL (3.9 and 5.2 mmol/L) and a fasting plasma triglyceride (TG) concentration less than 200 mg/dL (<2.3 mmol/L). Hyperlipidemic subjects were screened for an initial fasting plasma TC concentration greater than 240 mg/dL (>6.2 mmol/L), fasting plasma TG concentration greater than 200 mg/dL (>2.3 mmol/L), and no lipid-lowering drug therapy within the past month. All subjects had been on regular thrice-weekly maintenance hemodialysis therapy for at least 1 year, with no intercurrent illness and a normal fasting plasma glucose concentration. Exclusion criteria were the presence of liver disease, thyroid disease, severe hypertension, or cancer and the use of any medication known to affect lipid concentrations. Primary end points of the study are changes in lipid, lipoprotein, and apolipoprotein concentrations. The protocol was approved by the Human Investigation Review Committees of Cathay General Hospital and Taipei Medical University. All subjects were informed about the study and provided written informed consent before beginning the study. Subjects who failed to comply with the diet or had a weight variation of 3 kg or greater during the study were excluded from the final analysis.

Of 46 patients screened, 42 patients gave their informed consent, and 39 subjects completed the study. Three patients withdrew from the study because of gastrointestinal problems (eg, constipation, diarrhea, nausea, and gastrointestinal upset). Two subjects who failed to consume the assigned protein dose (1.2 g/kg/d), as assessed by the dietitian, were excluded from statistical analyses. Nineteen hyperlipidemic and 18 normolipidemic subjects completed the study and were included in statistical analyses. We chose subjects with hyperlipidemia and normolipidemia to examine effects of soy protein in hemodialysis patients in accordance with following reasons.

1. Initial serum cholesterol concentrations had a powerful effect on changes in serum TC and low-density lipoprotein cholesterol (LDL-C) concentrations.[7] Serum cholesterol level increases greater than 240 mg/dL (>6.2 mmol/L) have been implicated as a risk factor for cardiovascular heart disease. For these reasons, we chose subjects with serum cholesterol levels greater than 240 mg/dL (>6.2 mmol/L) to potentially maximize the effect of soy protein.
2. The hypocholesterolemic effect of soy protein also was shown in normocholesterolemic subjects with normal renal function. There are reports in the literature that maintenance hemodialysis patients with low-normal (<150 mg/dL [<3.9 mmol/L]) serum cholesterol levels have greater mortality than those with greater cholesterol levels.[18] Therefore, we examined the effect of soy protein on hemodialysis patients with normal serum cholesterol concentrations (150 to 200 mg/dL [3.9 to 5.2 mmol/L]) to evaluate whether soy protein would decrease serum cholesterol levels to a range lower than normal.
3. Patients with a serum cholesterol concentration between 200 and 240 mg/dL are not the primary target population of cholesterol-lowering therapy. Diet modifications (low-fat, low-cholesterol) have been shown to decrease serum cholesterol levels by approximately 14%.[19] In this population, a change in eating pattern could achieve a desirable lipid level, in our experiences. Thus, we did not include patients with serum cholesterol concentrations of 200 to 240 mg/dL (5.2 to 6.2 mmol/L) in the present study.

Study Design and Diet

During a 4-week run-in phase, all subjects followed the usual hemodialysis diet (35% fat, 1.2 g/kg/d of protein, and ~32 to 35 kcal/kg/d of energy). A registered dietitian instructed subjects on this diet and counseled them about their individual needs for protein, fat, and energy. After the run-in phase, baseline blood samples were drawn and subjects in each category (hyperlipidemic or normolipidemic) were randomly assigned to 1 of 2 dietary treatment subgroups that provided isolated soy protein (ISP) or milk protein (control group). For 12 weeks, all subjects continued to consume the usual hemodialysis diet and were asked to consume one 30-g packet of ISP (Supro 660; Protein Technologies Int, St Louis, MO) or one 30-g packet of milk protein (P93; Sentosa, BV, Holland) each day at breakfast (nondialysis day) or after dialysis (dialysis day). Individual dietary counseling was provided with the goal of making a dietary adjustment to incorporate the test protein into the diet without causing weight gain or changes in protein or energy intake. This requirement was reinforced at clinic visits and monitored during the study by reviewing dietary recalls.

Clinic visits were conducted every dialysis day. At each clinic visit, the study protein was delivered, and any leftover packets from the previous visit were collected to determine compliance. A 24-hour dietary recall was performed for all subjects for 3 days every 4 weeks. The 3 days included a dialysis day, a nondialysis day, and a Sunday. Compliance with dietary protein intake was measured by using the 24-hour dietary recall and calculating the protein equivalent of nitrogen appearance (PNA) from urea nitrogen appearance determination. ISP was fortified with calcium (calcium lactate) to amounts similar to those found in milk protein. Test products were formulated in sealed packets. The test products were isoenergetic and contained equal amounts of carbohydrate and fat to provide similar calories to those found in 30 g of meat protein. It was suggested that the test product be mixed with 200 mL of water or soup, and shakers were provided for mixing purposes. Throughout the study, all subjects were asked to maintain their edema-free body weight and take no nutritional supplements for the duration of the investigation. No lipid-lowering drug therapy or medication known to affect lipid concentration was used during the trial period. Subjects, study staff, and laboratory